International Application No PCT/GB2004/002893

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/00 A61K9/00 A61K31/135 A61K31/485 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) A61M A61K IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. P.X WO 03/070304 A (G W PHARMA LTD ; DAVE 1-3,7,9, RAJIV BOBBY (GB)) 22-24,35 28 August 2003 (2003-08-28) page 8, line 33 - page 13, line 6 page 19, line 18 - page 25, line 27; figures WO 02/32487 A (RIDDIFORD MARTIN PHILIP; G Y 1-13, W PHARMA LTD (GB); DAVE RAJIV BOBBY (GB);) 15-18, 25 April 2002 (2002-04-25) 22-24,35 abstract; claims; figures Y EP 0 672 416 A (EURO CELTIQUE SA) 1-3,7-9 20 September 1995 (1995-09-20) 22-24,35 abstract; claims; example 1 Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the lengths. "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the International "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to Involve an inventive step when the document is taken alone fliing date "L" document which may throw doubts on priority daim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 0 1 12 2004 29 September 2004 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Hijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 Vänttinen. H

International Application No PCT/GB2004/002893

		1017 00200	147002093
C.(Continua	tion) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
Υ.	WO 03/037306 A (WHITTLE BRIAN ANTHONY; GW PHARMA LTD (GB)) 8 May 2003 (2003-05-08) page 4, line 1 - page 8, line 36; example 2; table 1 page 22, line 29 - page 23, line 21 page 25, line 4 - page 26, line 3; claims		10-13, 15-18
Υ	US 3 980 766 A (SHAW IRVING F ET AL) 14 September 1976 (1976-09-14) the whole document	٠.	4-6
	·		

International application No. PCT/GB2004/002893

Box il Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 29,31,32 because they relate to subject matter not required to be searched by this Authority, namely:
It is unclear which technical features form the subject-matter of claim 29, because claims 13-16 and 18-21 relate to a dispenser and claim 29 refers to a formulation of said claims.Claims 31 and 32: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
Claims Nos.: because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this International application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were pald, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-24, 35
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-24,35

Dispenser having a reservoir and a method for making the

2. claims: 25-28,30,33,34

Diamorphine formulation and its use

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 29,31,32

It is unclear which technical features form the subject-matter of claim 29, because claims 13-16 and 18-21 relate to a dispenser and claim 29 refers to a formulation of said claims.
Claims 31 and 32: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

information on patent family members

International Application No
PCT/GB2004/002893

				1017 452	0047002033
Patent docume cited in search re		· Publication date		Patent family member(s)	Publication date
WO 0307030)4 A	28-08-2003	GB GB CA EP WO GB	2385845 A 2385846 A 2475357 A1 1478420 A1 03070304 A1 2391857 A ,B	03-09-2003 03-09-2003 28-08-2003 24-11-2004 28-08-2003 18-02-2004
WO 023248	7 A	25-04-2002	GB AU CA EP WO JP US	2368061 A 9577101 A 2426101 A1 1328309 A1 0232487 A1 2004511310 T 2004069798 A1	24-04-2002 29-04-2002 25-04-2002 23-07-2003 25-04-2002 15-04-2004
EP 067241	6 A	20-09-1995	EP GBP UUA A A A A A A A A A A A A A B B B B B	0654263 A1 2287880 A 0672416 A1 694475 B2 1475595 A 2144500 A1 951155 A 8040905 A 950950 A 5843480 A 3413 U2 138566 T 172376 T 212224 T 201989 T 3995797 A 722358 B2 5299598 A 6196394 A 6610594 A 682223 B2 7901594 A 62473 B1 99077 A 62473 B1 99078 A 62429 B1 99198 A 2123160 A1 2127166 A1 1099262 A 110521 A 9401093 A3 9401550 A3 9401550 A3 9402866 A3 9422335 U1 69400215 D1 69400215 T2 69414046 D1 69427472 D1 69427472 T2	24-05-1995 04-10-1995 20-09-1995 23-07-1998 21-09-1995 15-09-1995 15-09-1995 15-09-1995 01-12-1998 27-03-2000 15-06-1996 15-11-1998 15-02-2002 15-06-2001 18-12-1997 27-07-2000 26-03-1998 17-11-1994 12-01-1995 31-08-1999 30-06-1995 31-08-1999 30-12-1999 28-07-1995 30-11-1999 28-08-1995 11-11-1994 02-01-1995 10-05-1995 10-05-1995 14-02-1996 16-11-1994 18-01-1995 14-06-1995 14-06-1995 14-06-1995 14-06-1995 14-06-1995 14-06-1995 14-06-1995 14-06-1996 26-11-1998 22-04-1999 19-07-2001 08-11-2001

Information on patent family members

International Application No
PCT/GB2004/002893

Patent document cited in search report	Publication date		Patent family member(s)	Publication . date
EP 0672416 A	,	DE DE DE DK DK DK	69429710 D1 69429710 T2 699436 T1 729751 T1 624366 T3 636370 T3 654263 T3	14-03-2002 08-08-2002 10-04-1997 13-03-1997 01-07-1996 28-06-1999 29-04-2002
WO 03037306 A	08-05-2003	GB EP WO	2381450 A 1439827 A2 03037306 A2	07-05-2003 28-07-2004 08-05-2003
US 3980766 A	14-09-1976	US	3885027 A	20-05-1975

PATENT COOPERATION TREATY

PCT

REC'D 1 2 SEP 2005

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SCB63535WO00	FOR FURTHER ACTION	See Form PCT/IPEA/416				
International application No. PCT/GB2004/002893	International filing date (day/month/year) 06.07.2004	Priority date (day/month/year) 07.07.2003				
International Patent Classification (IPC) or na A61M15/00, A61K9/00, A61K31/135	utional classification and IPC , A61K31/485	1				
Applicant GW PHARMA LIMITED et al.						
This report is the international prel Authority under Article 35 and tran	liminary examination report, establishensmitted to the applicant according to A	ed by this International Preliminary Examining Article 36.				
2. This REPORT consists of a total of	of 7 sheets, including this cover sheet.	•				
3. This report is also accompanied by	y ANNEXES, comprising:					
a. 🛛 sent to the applicant and to	the International Bureau) a total of 3	sheets, as follows:				
sheets of the description and/or sheets containing Administrative Instruction	on, claims and/or drawings which have ng rectifications authorized by this Autr ions).	be been amended and are the basis of this report hority (see Rule 70.16 and Section 607 of the				
sheets which supersed beyond the disclosure Supplemental Box.	beyond the disclosure in the international application as filed, as indicated in item 4 of Pare No.					
	b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplementa Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).					
4. This report contains indications rel	ating to the following Items:					
☐ Box No. I Basis of the opin	nion					
☐ Box No. II Priority						
☐ Box No. III Non-establishme	ent of opinion with regard to novelty, In	nventive step and industrial applicability				
Box No. IV Lack of unity of i	nvention					
approability, ona	ment under Article 35(2) with regard to tions and explanations supporting suc	novelty, inventive step or industrial ch statement				
☐ Box No. VI Certain documer						
☐ Box No. VII Certain defects	n the international application					
LI BOX NO. VIII Certain observat	Box No. VIII Certain observations on the international application					
Date of submission of the demand	Date of complet	tion of this report				
06.05.2005	09.09.2005					
Name and mailing address of the international preliminary examining authority:	Authorized Office	cer				
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 52365 Fax: +49 89 2399 - 4465	·	+49 89 2399-7442				

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/GB2004/002893

_	•	·					
_	Box No. I Basis of the report						
1.	 With regard to the language, this report is based on the international application in the language in which it wa filed, unless otherwise indicated under this item. 						
	international search (und	slations from the original language into the following language, anslation furnished for the purposes of: er Rules 12.3 and 23.1(b)) tional application (under Rule 12.4) examination (under Rules 55.2 and/or 55.3)					
2.	With regard to the elements* of	the international application, this report is based on (replacement sheets which					
	Description, Pages						
	1-24	as originally filed					
	Claims, Numbers						
	1-22	received on 06.05.2005 with letter of 04.05.2005					
	Drawings, Sheets						
	1/7-7/7	as originally filed					
	☐ a sequence listing and/or any	y related table(s) - see Supplemental Box Relating to Sequence Listing					
3.	☐ The amendments have result the description, pages the claims, Nos. ☐ the drawings, sheets/figs the sequence listing (specially any table(s) related to sec	cifv):					
4.	☐ This report has been established.	shed as if (some of) the amendments annexed to this report and listed below ave been considered to go beyond the disclosure as filed, as indicated in the					
	* If item 4 applies, so	me or all of these sheets may be marked "superseded "					

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/GB2004/002893

		•				
	Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability					
1.	The obv	questions whether the claimed ious), or to be industrially applica	inver able l	ntion appears to be novel, to involve an inventive step (to be non- have not been examined in respect of:		
!		the entire international applicati	on,			
!		claims Nos. 17-21				
		because:				
	×	the said international applicatio does not require an international	n, or al pre	the said claims Nos. 18-21 relate to the following subject matter which eliminary examination (specify):		
		see separate sheet				
	⊠	the description, claims or drawi unclear that no meaningful opin	ngs ((indicate particular elements below) or said claims Nos. 17 are so could be formed (specify):		
		see separate sheet				
		the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.				
	\boxtimes	no international search report h	as b	een established for the said claims Nos. 17-21		
		the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:				
		the written form		has not been furnished		
				does not comply with the standard		
		the computer readable form		has not been furnished		
				does not comply with the standard		
		the tables related to the nucleonot comply with the technical re	tide : equir	and/or amino acid sequence listing, if in computer readable form only, do ements provided for in Annex C-bis of the Administrative Instructions.		
		See separate sheet for further details				

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/GB2004/002893

	Box	No. IV Lack of unity of inv	ention			
1.		In response to the invitation to ☐ restricted the claims. ☐ paid additional fees. ☐ paid additional fees under ☐ neither restricted nor paid	protest		litional fees, the applicant has:	
2.		This Authority found that the Rule 68.1, not to invite the ap	requirer plicant	nent of unity to restrict or	of invention is not complied with and chose, according to pay additional fees.	
3.	. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is					
		complied with.				
		not complied with for the follo	wing re	asons:		
4.	Co	nsequently, this report has bee	en estab	olished in res	spect of the following parts of the international application:	
	\boxtimes	all parts.				
		the parts relating to claims N	os			
		x No. V Reasoned statements Reasoned statements Reasoned Statements Reasoned Statements Reasoned Reaso	ent und lanatio	er Article 3 ns support	5(2) with regard to novelty, inventive step or industrial ing such statement	
1.	Sta	atement				
	No	velty (N)	Yes: No:	Claims Claims	1-16,22	
	lnv	rentive step (IS)	Yes: No:	Claims Claims	1-16,22	
	Inc	dustrial applicability (IA)	Yes:		1-16,22	
		, to y	No:	Claims	, .,	
2.	Cit	ations and explanations (Rule	70.7):			
	se	e separate sheet				
_	Box No. VII Certain defects in the international application					

The following defects in the form or contents of the international application have been noted:

see separate sheet

1 Concerning Item III

- 1.1 It is unclear which technical features form the subject-matter of claim 17, because claims 9-12 relate to a dispenser and claim 17 refers to a formulation of said claims. Consequently and because said claim has not been searched, it cannot be examined in respect of Article 33(2)-(4) PCT.
- 1.2 Claims 18-21 fall under Rule 67.1(iv), because they concern a method for treatment of the human or animal body by therapy. Consequently and because said claims have not been searched, they cannot be examined in respect of Article 33(2)-(4) PCT.

2 Concerning Item V

- 2.1 WO-A-02/32487 (D2) discloses a dispenser according to claim 1 without a mention about a "drug of abuse" contained in the reservoir. EP-A-0 672 416 (D3), WO-A-03/037306 (D4) and US-A-3 980 766 (D5) disclose that opiates and especially diamorphine or methadone may be advantageously administered orally. In the light of the combined teachings of D2 and D3, D4 or D5, it would be obvious for the skilled person to arrive at the subject-matter of claims 1-8. Thus, the subject-matters of claims 1-8 do not meet the requirement of Article 33(3) PCT.
- 2.2 In addition, the technical features and method steps of claims 14-16 and 22 are considered to be obvious from the combination of D2 and D3, the technical features of claims 9 and 10 from the combination of D2 and D4, and the technical features of claims 11-13 appear to relate merely to one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed. Consequently, said claims do not meet the requirement of Article 33(3) PCT.
- 2.3 Furthermore, for the entrance into the regional phase the attention of the applicant is drawn to WO-A-03/070304 (D1) which appears to disclose the subject-matters of claims 1-3, 7, 14-16 and 22 and has a priority date which is prior to the priority date of the present application.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET) International application No.

PCT/GB2004/002893

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.

PCT/GB2004/002893

2.4 The industrial applicability (Article 33(4) PCT) of a device according to the claims 16 and 22 appears to be self-evident.

3 Concerning Item VII

The closest prior art has not been identified as required by Rule 5(a)(ii) PCT. Furthermore, the independent claims are not in the two-part form as required by Rule 6.3(b) PCT. In addition, the claims do not include reference signs in parentheses as required by Rule 6.2(b) PCT.

CLAIMS

- 1. A dispenser comprising a reservoir containing a plurality of dosage units each of which comprise a formulation of a controlled drug or drug of abuse, said dosage units being contained in a tamper-evident manner such that access to the dosage units in use is controlled either by the dispenser or remotely and/or is monitored either by the dispenser or remotely.
- 2. The dispenser as claimed in claim 1, wherein the controlled drug or drug of abuse is a class A drug in a non-intravenous formulation, as defined by The Misuse of Drugs Act 1971.
- 3. The dispenser as claimed in claim 1 or 2, wherein the controlled drug or drug of abuse is an opioid.
- 4. The dispenser as claimed in any one of the preceding claims, wherein the opioid is methadone or a pharmaceutically acceptable salt or derivative thereof.
- 5. The dispenser as claimed in claim 4, wherein the opioid is methadone hydrochloride.
- 6. The dispenser as claimed in claim 4 or claim 5, wherein the formulation is for oral delivery.
- 7. The dispenser as claimed in any one of claims 1 to 3, wherein the opioid is diamorphine or a pharmaceutically acceptable salt or derivative thereof.
- 8. The dispenser as claimed in claim 7, wherein the opioid is diamorphine hydrochloride.

- 9. The dispenser as claimed in claim 7 or 8, wherein the formulation is dry and suitable for nasal delivery upon mixing with an aqueous solution.
- 10. The dispenser as claimed in claim 9, wherein the formulation further comprises a solubility enhancer.
- 11. The dispenser as claimed in claim 10, wherein the solubility enhancer is one or more of caffeine, sodium benzoate and sodium salicylate.
- 12. The dispenser as claimed in claim 10 or claim 11, wherein the solubility enhancer comprises caffeine and sodium benzoate and / or sodium salicylate.
- 13. The dispenser as claimed in any one of claims 9 to 12, wherein said formulation is a freeze-dried formulation.
- 14. The dispenser as claimed in any preceding claim, wherein more than 1 day's supply of dosage units are contained in the dispenser.
- 15. A reservoir as claimed in any one of claims 1 to 14, for use in the dispenser of claim 1.
- 16. A method of making a dispenser as defined in any one of claims 1 to 15, comprising introducing the plurality of dosage units into the reservoir and then sealing the reservoir in the dispenser so as to render the dispenser tamper-evident.

- 17. A formulation as defined in any one of claims 9 to 12.
- 18. A controlled method of taking a drug of abuse or a controlled drug comprising administering said drug of abuse or controlled drug from a dispenser as defined in any one of claims 1 to 14.
- 19. A method as claimed in claim 18, wherein said drug of abuse or controlled drug is present in a formulation as defined in any one of claims 9 to 12.
- 20. Use of a drug of abuse or a controlled drug in the manufacture of a medicament for use in a controlled method of taking a drug of abuse or controlled drug comprising administering said drug of abuse or controlled drug from a dispenser as defined in any one of claims 1 to 14.
- 21. Use as claimed in claim 20, wherein said drug of abuse or controlled drug is present in a formulation as defined in any one of 9 to 12.
- 22. A kit of parts comprising a dispenser as claimed in any one of claims 9 to 12; and aqueous liquid for introduction into the dispenser for rendering the formulation suitable for nasal administration.

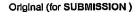
633366; NLW, NLW



PCT REQUEST

Original (for SUBMISSION)

ti	Declaration: Inventorship (only for the purposes of the designation of the United States of America)	
ti ti 0 4		I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought. This declaration is directed to the international application of which it forms a part (if filing declaration with application). I hereby declare that my residence, mailing address, and citizenship are as stated next to my name. I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications", by application number, country or Member of the World Trade Organization, day, month, and year
		of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international
		application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.
VIII-4-1-	Prior applications:	0315861.5, GB, 07 July 2003 (07.07.2003



I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

VIII-4-1- 1-2	Residence: (city and either US State, if applicable, or country)
VIII-4-1- 1-3	Mailing address:
VIII-4-1- 1-4	Citizenship:
VIII-4-1- 1-5	Inventor's Signature: (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)
VIII-4-1- 1-6	Date: (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international

VIII-4-1- Name (LAST, First)

application)

WHITTLE, Brian A.

Salisbury, United Kingdom

Porton Down Science Park, Salisbury, Wiltshire, SP4 0JQ, United Kingdom GB

> Glwhul 12 July 2004

Original (for SUBMISSION)

VIII-4-1- 2-1	Name (LAST, First)	DAVE, Rajiv B.
2-2	Residence: (city and either US State, if applicable, or country)	Salisbury, United Kingdom
VIII-4-1- 2-3	Mailing address:	Porton Down Science Park, Salisbury, Wiltshire, SP4 0JQ, United Kingdom
VIII-4-1- 2-4	Citizenship:	GB /
VIII-4-1- 2-5	Inventor's Signature: (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)	/ spi/h
VIII-4-1- 2-6	Date (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)	20/1/04.